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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WORTMAN, DONNA C	
ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 12/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,277	BRANCH ET AL.	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-30 and 32-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to comply, seq.* .

Claims 1-11, 19-23, 26, 27, and 30 were amended and new claims 31-35 were added in Paper No. 11.

As amended, this application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I, claims 1-23, 25, 27, and 32-34, insofar as drawn to polypeptides encoded by HCV +1 reading frame, nucleic acid encoding the polypeptides, corresponding vaccine composition, and method of use.

Group II, claims 1-4, 10, 14-16, 25, and 34, insofar as drawn to polypeptides encoded by HCV +2 reading frame, vaccine composition, and method of use.

Group III, claims 19-21 and 27, insofar as drawn to nucleic acid encoding polypeptides encoded by HCV +2 reading frame, vaccine composition, and method of use.

Group IV, claims 24, 26, and 35, insofar as drawn to an antibody to a polypeptide encoded by HCV +1 reading frame.

Group V, claims 24, 26, and 35, insofar as drawn to an antibody to a polypeptide encoded by HCV +2 reading frame.

Group VI, claims 28 and 31, insofar as drawn to a method of detecting antibodies to an HCV +1 reading frame polypeptide.

Group VII, claim 28 and 31, insofar as drawn to a method of detecting antibodies to an HCV +2 reading frame polypeptide.

Group VIII, claims 29 and 31, insofar as drawn to a method of detecting an HCV +1 polypeptide.

Group IX, claims 29 and 31, insofar as drawn to a method of detecting an HCV +2 polypeptide.

Group X, claim 30, insofar as drawn to a method of identifying a compound that binds to an HCV +1 polypeptide.

Group XI, claim 30, insofar as drawn to a method of identifying a compound that binds to an HCV +2 polypeptide.

The inventions listed as Groups I-XI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of Group I is the existence of HCV +1 frameshift polypeptides, the nucleic acid encoding HCV +1 polypeptides, and a method of using the polypeptides and nucleic acid as a vaccine. The claims of Groups II-V are drawn to additional products that are distinct from the product of Group I. The claims of Groups VI-XI are drawn to methods that are different from the method of Group I in that they require different products and/or different process steps and/or have different goals and outcomes. PCT Rule 13 does not provide for multiple products and methods.

Applicant's election with traverse of original Group VIII, claim 29, in Paper No. 11 is acknowledged. Group VIII now comprises claim 29 as amended and new claim 31, insofar as each claim is drawn to a method of detecting an HCV +1 polypeptide. The traversal is on the ground(s) that there was no holding of lack of unity in the international stage, that Groups VI, VII, VIII and IX should be rejoined into a single group, that claim 31 is an allowable 'generic' claim, and that a species election might be proper since claim 31 is now in the case. This is not found persuasive because Applicant has not addressed the specific reasons given for holding lack of unity, particularly that a polypeptide from an HCV +1 reading frame is a different product from a polypeptide from an HCV +2 reading frame. It is noted that the expression "special technical features" when applied to lack of unity consideration in PCT and 371 practice means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. It is not understood how prior art that anticipates or makes obvious one polypeptide would necessarily anticipate or make obvious a completely different polypeptide. Further, since Applicant has not stated on the record that any prior art that anticipates or makes

obvious the elected invention insofar as drawn to detection of an HCV +1 reading frame polypeptide identically anticipates or equally makes obvious the detection of an HCV +2 reading frame polypeptide, it is maintained that each polypeptide is distinct and makes a separate contribution over the prior art. Additionally, a polypeptide and the antibody that specifically binds it are distinct products, not species of the same genus of products. A method of detecting a specific antibody is a different process from a method using an antibody to detect a polypeptide; it is not understood how two different processes could be species of a single genus. Applicant has not addressed the observation that PCT Rule 13 does not provide for multiple products and methods.

The requirement is still deemed proper and is therefore made FINAL.

This application is not in compliance with the sequence rules, 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. In particular, the Application contains sequences that are not accompanied by the required SEQUENCE ID NO's as set out in 37 CFR 1.821(d). See, e.g., pages 12, 21, 35, and Table 1. Applicant is requested to return a copy of the attached Notice to Comply with the reply. Applicant is given the same time period in which to comply with the sequence rules as is available to reply to this Office action.

Claims 29 and 31, insofar as drawn to a method of detecting an HCV +1 polypeptide, are under examination at this time. Claims 1-28, 30 and 32-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being

drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

Claims 29 and 31 are objected to because of the following informalities: Claims 29 and 31 are objected to as reciting, depending from, or reading on non-elected subject matter. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 29 recites diagnosing HCV infection by detecting the polypeptide of claim 1 in the body fluid or tissue of a subject. Claim 1 recites "An isolated or recombinant polypeptide comprising an amino acid sequence encoded by an alternate reading frame." Since the specification does not describe a method of diagnosing HCV infection by detecting an "isolated or recombinant" polypeptide of any sort in the body fluid or tissue of a subject, one skilled in the relevant art would not reasonably recognize that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 29 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 29 and 31 are under examination insofar as they are drawn to a method of detecting an HCV +1 polypeptide in the body fluid or tissue (claim 29) or in the body fluid (claim 31) of a subject. The specification teaches, in Examples 1 and 2, that polypeptides derived from an HCV +1 reading frame detect antibodies that are present in the body fluid of subjects infected with HCV. While the specification teaches that one can use such polypeptides to raise antibodies that may subsequently be used to detect polypeptides in tissue or body fluids of infected subjects (pages 20-25), the specification does not provide results of such assays that would serve to demonstrate that such polypeptides are actually circulating or present in the body fluids of infected subjects, or that antibodies raised against the disclosed polypeptides actually detect HCV +1 reading frame polypeptides in body fluids or tissues of infected subjects. While methods for raising antibodies and methods for using antibodies to detect polypeptides in conventional immunoassay formats are described, an actual antibody raised against the disclosed polypeptides and an immunoassay that in fact detects the presence of HCV +1 reading frame polypeptide in an infected subject is not described in such a way that one of skill would be able to practice the invention without undue experimentation. In this regard, while the detection of antibodies in patient sera to an HCV +1 viral polypeptide may imply that the polypeptide may be expressed during infection at least in some patients (see, e.g., Varaklioti et al., The Journal of Biological Chemistry 20:17713-17721, 2002,

cited on PTO 892, attached), and while patient antisera apparently detect an HCV +1 polypeptide in transfected cell lysates, no structural or functional role for the protein has been described in the viral life cycle, and neither the actual expression of the polypeptide in different HCV isolates during infection *in vivo* nor the presence of the polypeptide in any type of tissue or body fluid sample has been demonstrated either in Applicant's specification, which claims priority to June 1998, or subsequently, using methods that are commensurate with those disclosed by Applicant. See Varaklioti, page 720, last four paragraphs. Lacking direct evidence that an HCV +1 reading frame polypeptide is present in the body fluid or tissue of an HCV infected subject, the specification cannot be said to enable one of skill in the art to practice the invention at the time the invention was made, without undue experimentation and with a reasonable expectation for success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is confusing because it is drawn to "A method of diagnosing HCV infection comprising detecting the presence or absence of the polypeptide of claim 1 ...". Claim 1 is drawn to "An isolated or recombinant polypeptide ...". It is not understood how one could diagnose a presumably naturally occurring viral

infection by detecting either an "isolated" or a "recombinant" polypeptide in a patient sample. Clarification is needed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Lo et al. (Virology 199:124-131, 1994), cited by

Applicant on PTO 1449 as Ref. B1, or Lo et al. (Virology 213:455-561, 1995), cited on PTO 1449 as Ref. B2, either in light of Xu et al. (The EMBO Journal 20(14):3840-3848, 2001), cited on PTO 1449 as Ref. B8. Lo B1 discloses the expression of an HCV protein from HCV core sequences that is referred to as P16 and its detection with a mouse monoclonal antibody and suggests that the protein is likely to be produced in vivo during HCV infection (see, e.g., Lo B1 page 129, page 126, "Comparative expression of the core gene products of two different HCV isolates"; second full paragraph under "DISCUSSION"). Lo B2 discloses that P16 and P21, the known HCV core protein, are co-amino terminal and that P16 is found as a nuclear protein when CV1 cells are transfected with an HCV core expression plasmid and detected with rabbit anti-core antibody. While neither Lo B1 nor Lo B2 discloses the P16 as being an HCV +1 reading frame polypeptide, both disclose it as a protein of interest in HCV infection and both disclose detecting it in an immunoassay. Xu et al., published subsequent to Applicant's filing date, disclose that P16 as taught by Lo B1 or Lo B2 is an HCV frameshift protein that reasonably appears to be the same HCV +1 polypeptide disclosed by Applicant. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have detected the HCV P16 of Lo B1 or of Lo B2 in the body fluid or tissue of a subject by immunoassay and to correlate the presence of HCV P16 with the presence of HCV infection because both Lo B1 and Lo B2 disclose the HCV P16 as a polypeptide that is specifically associated with the expression of HCV core nucleotide sequence. In detecting HCV P16, one would necessarily have detected HCV +1 reading frame

polypeptide as instantly claimed because Xu et al. disclose that P16 comprises an HCV +1 reading frame polypeptide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
December 15, 2002